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TITLE: **Testosterone Combined with Electrical Stimulation and Standing: Effect on Muscle and Bone**

PRINCIPAL INVESTIGATOR(S): **GAIL F. FORREST, Ph. D.**

CONTRACTING ORGANIZATION: **Kessler Foundation**
West Orange, NJ 07052

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Gail F Forrest Ph.D;

E-Mail: gforrest@kesslerfoundation.org

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Kessler Foundation

300 Executive Drive, Suite 70
West Orange, NJ 07052-3390

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14. ABSTRACT

The study is a prospective, randomized, double blinded, controlled, multi-site clinical trial to determine the efficacy of a tri combination intervention to improve musculoskeletal gains in men with subacute to chronic SCI with low circulating testosterone levels. Participants will be enrolled at Kessler Foundation (KF), the University of Louisville-Frazier Rehab (UoL), the James J. Peters VA Medical Center (JJPVAMC). During year 1 of the study, the Study Team (Drs. Forrest, Bauman, and Harkema) established a new partnership with a pharmaceutical company (AbbVie) to supply Drug and Placebo for all potential study participants. Each of the study sites submitted to the pharmaceutical company all requested regulatory documentation. Manufacture of the drug/placebo with randomization across the sites for administration of drug/placebo will be completed in early Year 2 of the study. Kessler submitted all required documentation to the FDA to obtain an IND number and approval for the use of drug/placebo and electrical stimulation, as specified in the study protocol. Kessler purchased electrical stimulators for use at the study sites. Local IRB approval at KF was completed. IRB approvals at UoL and JJPVAMC are pending. The Manual of Operation Procedures and the Case Report Forms have also been completed.

15. SUBJECT TERMS
Muscle atrophy and osteoporosis after SCI. Testosterone, placebo, multi muscle electrical stimulation, dynamic standing protocol, tri combination intense therapeutic training.

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1. INTRODUCTION

This study is a prospective, randomized, double blinded, controlled, multi-site clinical trial to determine the effectiveness of a tri combination Activity-Dependent Rehabilitation Model on improving musculoskeletal gains in men with subacute to chronic SCI who have low serum testosterone levels. A total of 56 research participants will be enrolled across 3 clinical sites: Kessler Foundation Research Center, the University of Louisville-Frazier Rehab and the James J. Peters VA Medical Center (Bronx, NY). Each site will recruit 20 participants over 3 years or 6-7 subjects per year. Eligibility will be determined by the site physician and site PI. Research participants will be randomized into one of four groups: 1) Stand Training only; 2) Stand+Electrical Stimulation; 3) Stand Training+Testosterone; 4) Stand Training+Testosterone+Electrical stimulation. Each research participant will complete 60 sessions of training.

The model involves intense training with testsoterone replacement therapy and electrical stimulation on multiple muscles. Our primary focus is to examine the change in muscle, but we will also look at the change in bone. This tri combination Activity-Dependent Rehabilitation Model can easily be adapted to a clinic based model.

2. KEYWORDS

Testosterone, multi muscle electrical stimulation, dynamic standing protocol, muscle volume, MRI, bone mineral density, DXA, QCT scans, blood markers, urine markers, 60 sessions of training, sub acute to chronic SCI.

3. ACCOMPLISHMENTS

- **What were the major goals of the project?**

Aims of Proposal

The overall aim of this proposal is to determine the interaction of testosterone, ES of multiple leg muscles and stand training or loading (bearing of the body weight) in individuals with sub-acute to early chronic SCI who are wheelchair reliant at least 75% of the time in a phase I/II multi-site randomized clinical trial (n=56, recruited at 3 training sites) on bone and muscle.

Our primary aim is to assess the effects of our novel tri combination Activity-Dependent Rehabilitation model approach on muscle volume of the lower limbs.

Our secondary aims are:

i) To better define the mechanisms that contribute to changes in muscle.

Secondary outcome measures associated with this aim will further assess whether the tri-combination of stand training with TRT and ES will lead to increased muscle strength and contractile elements of muscle as shown by an increase in muscle torque, an increased expression of PGC-1α and its downstream targets in the lower limb and an alteration in myostatin signaling. Preliminary data from animal studies have shown increased expression of Activin receptor IIB and increased nuclear localization of Smad2 and Smad3 after SCI and that these adverse changes are reversed by androgens. Additional studies will examine mRNA levels for myostatin, its receptor and its inhibitors (e.g., follistatins) and determine nuclear levels of Smad2 and Smad3. We will also measure resting energy expenditure to confirm that changes in muscles mass correspond to anticipated metabolic effects.

ii) To evaluate the changes in bone and bone structure with Stand Training with TRT and ES.

Secondary outcome measures of this aim will include BMD of the proximal tibia and distal femur; these are the most common sites for fracture and may also respond faster to intervention. Other secondary outcome measures will be BMD at the hip, cortical and trabecular bone with 3-D volumetric measurements, and bone markers for formation and resorption.

- **What was accomplished under these goals?**

In Year 1 we had a significant obstacle where we were informed that Watson Laboratories had been acquired by a company that would not be able to supply drug and placebo- the fill details are described below in Page 4. In addition – the sequential timeline to a positive solution for acquisition of drug/placebo is also explained in Page 5-6. Therefore the major accomplishment in Year 1 was on November 10th, 2015 we received notification from Abbvie that they will provide the drug and placebo at no cost to the study. Drs. Forrest and Bauman contacted Dr. Henry on November 11, 2015 to notify her of our final solution. All of these details are described on Page 4-6.

In year 1 we did accomplish local IRB at Kessler for original protocol but we placed all IRB submissions and resubmissions on hold until we organized a suitable solution for drug acquisition. In Year 2 quarter 1 we received local IRBs at JJPVAMC and Kessler (UoL, pending).

Specific Aims: (1) To examine the effectiveness of stand training with testosterone and electrical stimulation to induce positive changes in muscle volume. **Our secondary aims are:** i) To better define the mechanisms that contribute to changes in muscle. ii) To evaluate the changes in bone and bone structure with Stand Training with TRT and ES.
Note we will start **modifying our IRB to show new protocol changes in November/ October 2015.**

As per SOW	**Timeline**
Major Task 1: Adapt TRT to ES protocol: Complete IRB	
Subtask 1: Prepare Regulatory Documents and Research Protocol for Study 1	
Sites for IRB completions submitted ***Milestone Achieved:*** *Local IRB approval at Kessler; IRB at UoL ,* JJPMC is pending after several resubmissions**.** ***Note: UoL and JJPMC needed to wait for IND number (4/29/1) before submitting to IRB***	***UoL and JJPMC submitted 5/29/15***

Major Task 2: Training of protocol at Kessler	3-6
Manual of Operations (MOP) and Standard Operating Procedures for TRT and Case Report Forms completed	6/28/14
Forrest and Harkema trained site PTs on Combination ST+ES.	4/28/15 Kessler UoL
Dr William Bauman (WB) will train all sites to administer testosterone patch based on Standard Operating Procedures.	Ongoing
Regular biweekly Conference calls (Kessler, UoL, JJPMC) established to discuss study protocol, training and testing.	Ongoing
Milestone Achieved: *Kessler and UoL Research staff trained in standing and ES protocol*	

- **What opportunities for training and professional development has the project provided?**

Training in Year 1 involved the Kessler PTs working on the Project for preliminary training on using the multi muscle stimulators.

- **How were the results disseminated to communities of interest?**

Nothing to report

- **What do you plan to do during the next reporting period to accomplish the goals?**

In the next reporting period we plan to do the following:

The tasks that we intend to complete in the next year (8.25.16) as per the original SOW submitted are given below.

Note: *<u>The time line in the SOW (8.25.16) below will be revised in year 2</u>.**

Major Task 1: Adapt TRT to ES protocol: Complete IRB	Time line
Submit amendments, adverse events and protocol deviations as needed	As needed
Coordinate with Sites for annual IRB report for continuing review	Annually
Milestone Achieved: Local IRB approval at Kessler, UoL , JJPMC)	3 months
Major Task 2: Training of protocol at Kessler	3-6
Manual of Operations will be completed and sent to all sites one month prior to training	80% completed 9.31.15
Faghri will train all site PI and PTs on Electrical stimulation protocol (ES)	3
Forrest and Harkema will train all site PIs and PTs on Combination ST+ES	3
Dr William Bauman (WB) will train all sites on testosterone patch	3
Forrest, Harkema and Bauman will instruct all sites on protocol description per MOP	3
Milestone Achieved: Research staff trained	**Timeline**
Subtask 2: Site Visit to review training	4
Drs. Harkema and Forrest will visit the Bronx VAMC study site to provide review and potential additional instruction of the procedures for Stand Training with ES (January , 2015). This will be followed by conference calls	4
Milestone Achieved: Maintained protocol training and follow up at all sites.	4-5
Major Task 3: Participant Recruitment, Therapy, Participant Evaluation	25-30
Subtask 1: Data set up with initial subject at each site.	
Coordinate with Sites for all study steps, web data collection and database requirements	
Set up assessment measurements (already established at 2 sites – Kessler, UoL)	4-6
Milestone Achieved: 1st participant consented, screened and enrolled at all sites	4-6
Milestone Achieved: At all sites Study begins	4-6
Begin subject recruitment	4-30
Screen potential participants	4-30
Evaluate and assign participants to one of the four randomized groups	4-30
Outcome measures assessment at baseline time frame	4- 30
At all sites: Research participant complete 60 sessions of training frequency of 4 times per week (1.5-hour) followed by post testing and follow up (MRI, DXA)	4- 33
Milestone Achieved: Record data for year 1, 2, 3, into ITW database; Report	4-33

initial findings	
Milestone Achieved: Report findings from Clinical Trail	33-36
Major Task 6: Data Analysis	
Subtask 1: Coordinate with Sites & Data Core entry for monitoring data collection rates and data quality	4-33
Data analyses ongoing for outcome measures (Muscle volume, muscle torque, gene expression, myostatin signaling, BMD, bone and blood markers, volumetric measures of bone resting energy expenditure)	6-33
Milestone Achieved: Report results from data analyses	35-36

4. IMPACT

Nothing to report

5. CHANGES/PROBLEMS

- **Changes in approach**

No change in protocol in Year 1.

- **Actual or anticipated problems or delays and actions or plans to resolve them**

During the reporting period there were significant delays associated with acquisition and delivery of drug/placebo. These delays were reported in the quarterly reports. The delays are outlined in detail below:

As reported in Quarter 1, year 1 report the main problem to address for Quarter 1 in year 1 was that we were informed that* Watson Laboratories *had been acquired by a company that would not be able to supply drug and placebo for our proposed placebo-controlled RCT. For Quarter Year 2 report 2 (7/14/2015) we proposed a long term solution to the TRT/Placebo issue. For the Year 2, Quarter 1 report we proposed our final solution to the TRT/Placebo issue. All for year 1 is explained below.

- At the time of submission of our grant, Watson Laboratories had provided a letter of support which stated that this company would provide TRT patch and matching placebo for our study. The support being offered by Watson Laboratories was a continuation of previous collaboration with the company for similar work that was completed by Dr. William A. Bauman, co-principal investigator on the current grant, which addressed the safety and efficacy of TRT patch in a population of persons with chronic spinal cord injury at the James J. Peters VA Medical Center and The Kessler Institute for Rehabilitation, work which was published in *Hormones and Metabolic Research* in 2011. In our Quarter 1, Year 1 report we reported that Watson Laboratories was obtained by Actavis Pharmaceuticals, and management at the new company had informed us that they had decided not to provide study drug for our RCT, nor for any other RCTs at this time. It was inferred that their policy decision was based on a change in philosophy toward research initiatives which took into account the total cost of supplying matching placebo and the assumption of risk for any new study.

- After careful consideration and in discussion with Patricia Henry, PhD, Science Officer (discussions: 2/17/2015 and 4/1/2015) Drs. Forrest, Bauman, and Harkema addressed the problem in a satisfactory manner to maintain the study as designed and to make no changes to the SOW.

- In Quarter 1, we reported that the FDA approved New York based compound pharmacy "Metro Drugs" would be supplying the drug (Gel) and placebo to the sites, and we provided a letter from the company confirming this agreement. Shortly after we submitted the Quarter 1 report, we were informed by the New York State (NYS) DEA that the only suitable and legal option to supplying drug and placebo to our 3 study sites was FDA approved pharmacy that was located outside NYS because of stringent laws that prohibited the dispensing of any controlled substances by an appropriately licensed NYS pharmacy outside of the state. In actual practice, the testosterone/placebo preparation would be sent by the FDA pharmacy directly to the subjects.

- As you may appreciate, identifying a FDA compound pharmacy that has the experience and resources to supply both study drug and placebo, with an appropriate dispensing system in place, was an onerous task, and our main difficulty with initiating this study to date. A pharmacy was located and agreed to provide the investigators with drug and placebo. To do so required the investigators to pay for the cost of topical generic testosterone preparation (at approximately 25% the cost of Androderm) and for a placebo gel. The cost of these preparations had been provided in a previous email, as well as the other associated costs, including those of the cost of dispensing ($10,920), repacking ($6006), and shipping ($24,570), with a total final cost of the pharmacy to provide us with drug/placebo of over $100,000, an expense that were not budgeted prior to Watson Laboratories withdrawing their support for our proposal. Of note, the investigators decided that intramuscular preparations of testosterone were not physiologic (peaks and valleys in pharmacokinetics) and in the SCI population would be associated with a heightened risk of autonomic dysreflexia, potentially a life-threatening complication, if the injection is delivered below the level of lesion; administration of the intramuscular injection above the level of lesion may be associated with pain and discomfort upon transfers, which may limit mobility, reduce drug/placebo compliance, and increase drop-out rates. A total of 56 research participants is proposed to be studied in our proposal.

- The source of the drug was Belmar Pharmacies, a licensed non-resident pharmacy (license #30,649) and that is licensed with the DEA. **We did supply the letter in the Quarterly report 7/14/15.** The pharmacy would have supplied the patient-specific compounded testosterone or placebo, directly to patients based upon a valid prescription. To date, this company had been the only viable option after an exhaustive search of both Clinical Trials.gov and reaching out to other pharmacies. Drs. Forrest and Bauman worked with the company to set up the standard of operation procedures for dispensing the drug/placebo to study participants.

- Drs. Forrest and Bauman had been in discussions via email and conference calls (6/9/15; 6/15/15; 6/16/15) with Patricia Henry, Ph.D., Science Officer regarding the potential of additional funds to cover the additional cost of the drug. Based on our discussions, Dr. Henry instructed us to submit a formal request for additional funding (6/18/15).

- Drs. Forrest and Bauman submitted a formal request to the DOD for additional funding on 6/23/15. **Please see letter in report dated 7/14/15.**

- Of note - In January 2015, the investigators submitted a request to Abbvie to provide testosterone gel and matching placebo for our study. We considered this "option" to be a real possibility, albeit somewhat unlikely if one considers the length of time that our request had languished without resolution. However, our proposal continued to be actively considered. We suggested in our previous quarterly report (7/14/2015) if this company approved our request, then the investigators would proceed with the clinical trial without the need for additional financial support from the DoD.

- Fortunately, in November 10th, 2015 we received notification from Abbvie that they had agreed in principle to provide the drug and placebo at no cost to the study. Drs. Forrest and Bauman contacted Dr. Henry on November 11, 2015 to notify her of our final solution. Dr. Henry had requested that Dr. Forrest submit a revised SOW (attached) to Dr Henry on 11/23/15. Based on the revised SOW – we have amended the protocols at all institutions to comply with our proposed changes in drug formulation (e.g., patch to gel application), dosage, and origin of agent/placebo.

- Note: At end of Quarter 2, Year 2 Abbvie Inc have manufactured drug/placebo at no cost to the grant. Final contractual agreement between Kessler Foundation and Abbvie is currently being signed (4/24/16). All details associated with shipping of drug to each site, storage of drug, administration have been addressed in Q2**,** Year 2.

- **Changes that had a significant impact on expenditures**

Because of the unanticipated delay in our obtaining of drug/placebo, we have not spent the projected funds for Year 1. **These details were outlined both in our financial and quarterly reports.**

- **Significant changes in use or care of human subjects, vertebrate animals, biohazards, and/or select agents**

No significant change to human subjects

6. PRODUCTS

None to report

- **Publications, conference papers, and presentations**

None to report

7. PARTICIPANTS & OTHER COLLABORATING ORGANIZATIONS

- **Has there been a change in the active other support of the PD/PI(s) or senior/key personnel since the last reporting period?**

Nothing to report

- **What individuals have worked on the project?**

In the year 1 period individuals' have worked primarily on setting up the protocol, IRB submissions, Manual of Operation Procedure (MOP) and Case Report Forms (CRF).

Overall Submitting PI: Gail F Forrest Ph.D.
Co- PI: William Bauman Ph.D.

Individuals that have worked for at least 1 month (~160 hrs) in year 1.

Name: Milda Woods
Project Role: Study Coordinator, consultant
Nearest person month worked: 2.7months
Contribution to Project: Ms. Woods has worked continually with Dr Forrest in year 1:

i) in setting up initial IRB applications, approvals and resubmission of IRB forms for continual approvals at Kessler
ii) on all documents for submission and resubmission for FDA IND approval
iii) on all documentation for Abbvie Inc submission approval process,
iv) on all case report forms for subject binders for all site and Manual of Operations to be used at all sites.

- **What other organizations have been involved as partners?**

Site 2: University of Louisville (UoL)
Frazier Rehab Institute
220 Abraham Flexner Way, Suite 1506
Louisville, KY 40202
Site PI: Susan Harkema Ph.D.
Site 3: James J. Peters VA Medical Center (JJPVA)
130 West Kingsbridge Road
Bronx, NY 10468
Site PI: Ann Spungen. EdD. William Bauman.

In year 1 UoL and JJPVA worked on their IRB submission. IRB approval pending.

- **Has there been a change in the active other support of the PD/PI(s) or senior/key personnel since the last reporting period?**

Nothing to report

8. SPECIAL REPORTING REQUIREMENTS

QUAD CHARTS submitted in appendices

9. APPENDICES

PIs Bio has been included.

BIOGRAPHICAL SKETCH

NAME: Gail F Forrest	**POSITION TITLE:** Associate Director, Human Performance and Engineering Research (HPER).
eRA COMMONS USER NAME: **gfforrest**	

EDUCATION/TRAINING

INSTITUTION AND LOCATION	DEGREE *(if applicable)*	MM/YY	FIELD OF STUDY
Bachelor of Applied Science RMIT, Melb., Australia	B. App. Sc.	1979	Mathematic/Computing
Temple University, Philadelphia	Ph.D.	1/2001	Biomechanics
Post Doctoral Fellow, Kessler Foundation		1/2001-12/2002	Biomechanics

A. Personal Statement

I am currently an Associate Professor of Physical Medicine & Rehabilitation Rutgers New Jersey Medical School, Rutgers, NJ, an Assistant Director of the Human Performance and Engineering Laboratory, an Affiliated Faculty Department of Biomedical Engineering, New Jersey Institute of Technology, Newark, NJ, Member of the Graduate Faculty in Biomedical Science, University of Medicine and Dentistry of New Jersey, Newark, NJ. I am currently funded by multiple grants from the National Institute on Disability and Rehabilitation Research (NIDRR), Christopher and Dana Reeve Foundation, Department of Defense, Craig H. Neilsen Foundation and New Jersey Commission on Spinal Cord Research. Much of my research and grant funding is directed towards understanding neurological and musculoskeletal and neurological recovery for individuals following spinal cord injury (SCI). This grant is focused directly at understanding the musculoskeletal gains of tri combination activity based rehabilitation intervention to improve musculoskeletal gains in men with subacute to chronic SCI with low circulating testosterone levels.

B. Positions and Honors.

1.1.1 Positions and Employment

Prior to 1989	Mathematics and Computer Science Senior Level Teacher, Australia.
1989-1992	Corporate Consultant to Four Season Hotels (Daikyo Corporation), Australia and Japan.
1991-1992	Victoria University, Melbourne, Australia, Grad Dip. Biomechanics
1995-1997	Teaching Assistant - Human Anatomyand Biomechanics, Temple University.
1997-1998	Biomechanics Lecturer and Coordinator, Temple University.
1998-1999	Teaching Assistant – Physiology, Biomechanics, and Anatomy, Temple University
1999-2000	Research Assistant – “Dynamic Control of Head Stability in Older Adults” Grant (NIA # RO3), Physical Therapy Dept, Temple University.
2000-2002	Post Doctoral Fellow, Kessler Medical Rehabilitation Research and Education Corporation,West Orange, NJ.
2003-2007	Research Scientist II , Kessler Medical Rehabilitation Research and Education Corporation, West Orange, NJ.
2007- 2012	Interim Director, HPMAL , Kessler Foundation Research Center , West Orange, NJ.
2007- Date	Kessler site Director of the NeuroRecovery Network.
2012- 2014	Assistant Director Human Performance Engineering Laboratory, Kessler Foundation.
2012-Present	Director Neuroplasticity Laboratory.
2014-Present	Associate Director Human Performance Engineering Laboratory, Kessler Foundation.

University Appointments

5/2000-9/2000	Adjunct Professor Biomechanics, Physiology, – Temple University, University of Pennsivalia
1/2001-6/2005	Instructor, University of Medicine and Dentistry of New Jersey / New Jersey Medical School
7/5/05-present	Assistant Professor University of Medicine and Dentistry of New Jersey/New Jersey Medical Sc.

2011-Date	Affiliated Faculty Department of Biomedical Engineering, New Jersey Institute of Technology, Newark, NJ
2012- Date	Member of the Graduate Faculty in Biomedical Science, University of Medicine and Dentistry of New Jersey, Newark, NJ.
2013 –Date	Associated Professor of Physical Medicine & Rehabilitation. Rutgers New Jersey Medical School. Rutgers, the State University of New Jersey

Other Professional Experience

1999 - 2000	Research Assistant Dynamic Control of Head Stability, Agency NIH/NIA (RO3); (Ronita Cromwell, Ph.D., Principal Investigator)
2001 - present	Institutional Review Board Member Kessler Foundation
2004 - present	Reviewer for Journal of Neuroengineering and Rehabilitation
2005 - present	Reviewer of Journal of Rehabilitation Research and Development
2005 - present	Reviewer of Journal of Spinal Cord Medicine
2005 - present	Compliance Committee member (subcommittee of IRB)
2005 - present	Committee member for ACRM International task force
2005 - present	Reviewer, RESNA
2009 -present	Adhoc Reviewer NIH (2014/10 ZRG1 BBBP-Y (05),
2013-2014	Motor Function, Speech and Rehabilitation (MFSR) Study Section).
2012-present	Reviewer for Craig H Neilson Foundation
2013-present	Reviewer for Gait and Posture.
2015-2021	Reviewer NIH grants, Permanent study member Motor Function and Rehabilitation Study Section

C. Selected peer-reviewed publications (2012-2015)

1. **Forrest GF**, A, Cirnigliaro C. Muscle Activation during Exoskeleton Assisted Walking. Submitted to Archives of Physical Medicine and Rehabilitation 2015.
2. **Forrest, GF**, Harkema SJ, Angeli, CA. Trunk muscle activation and center of mass changes during loading for chronic motor complete SCI. Submitted Gait and Posture, 2015.
3. **Forrest, GF**, Harkema SJ, Angeli, CA, Kirshblum, S., Cirnigliaro, CM, Faghri, Garabrini, E., Bauman, W. Preliminary Results on the Differential Effect on Bone of Applying Multi-Muscle Electrical Stimulation to the Leg while Supine or Standing in Patients with SCI: The Importance of Combining a Mechanical Intervention with Gravitational Loading. Journal of Spinal Cord Medicine (Accepted, 2015).
4. **Forrest, GF,** Harkema SJ, Angeli, CA, Kirshblum, S., Cirnigliaro, CM, Faghri, Garabrini, E., Bauman, W. Preliminary Results on the Differential Effect on Bone of Applying Multi-Muscle Electrical Stimulation to the Leg while Supine or Standing in Patients with SCI: The Importance of Combining a Mechanical Intervention with Gravitational Loading. Journal of Spinal Cord Medicine (Accepted, 2015).
5. **Mitchell MD**, Yarossi MB, Pierce DN, Garbarini EL, Forrest GF. Reliability of surface EMG as an assessment tool for trunk activity and potential to determine neurorecovery in SCI. Spinal Cord. 2014 Dec 2. doi: 10.1038/sc.2014.171. [Epub ahead of print]
2. **Forrest GF,** Hutchinson K, Lorenz DJ, Buehner JJ, Vanhiel LR, Sisto SA, Basso DM. Are the 10 Meter and 6 Minute Walk Tests Redundant in Patients with Spinal Cord Injury?. PLoS One. 2014 May 1;9(5)/2014
3. Pilkar RB, Yarossi M, **Forrest G**. Empirical mode decomposition as a tool to remove the function electrical stimulation artifact from surface electromyograms: preliminary investigation. IEEE Engineering in Medicine and Biology Conference Proceedings 2012; 1847-50. doi: 10.1109/EMBC.2012.6346311.
4. **Forrest, GF,** Hudson, L, Basso, M, Behman, A, Harkema, SJ, Correlations among functional outcome measures in patients with incomplete spinal cord injury who are receiving activity-based rehabilitation. Archives of Physical Medicine and Rehabilitation. 2012 Sep;93(9):1553-64
5. Morrison, SA, **Forrest, GF**, VanHiel LR, DeLorenzo,D. NeuroRecovery Network Provides Standardization of Locomotor Training for Persons With Incomplete Spinal Cord Injury. Archives of Physical Medicine and Rehabilitation. 2012 Sep;93(9):1574-7.
6. Buehner J, **Forrest GF**, Schmidt, M, Tansey K, Basso M. Relationship between ASIA Exam and Functional Outcomes in the NeuroRecovery Network Locomotor Training Program. Archives of Physical Medicine and Rehabilitation. 2012 Sep; 93(9):1530-40.

Abstracts (2012-2015)

1.
2. **Forrest GF**, Ramanujam A, Pierce D, Johnson E, Garbarini E, Lamb R. Multi Muscle Neuromuscular Stimulation of the Lower Limbs: Effect on Motor Pools. Program No. 537.19. 2014. Neuroscience Meeting Planner. Washington, DC: Society for Neuroscience, 2014. Online
3. Bayram M, Mitchell M, Pilkar R, Barrance P, **Forrest GF**. Standing Biomechanics Of The Knee And Effect Of Electrical Stimulation On Muscle Response in SCI Adults. Soc Neurosci, Nov., 2014. Program Number 827.03/KK10. Neuroscience Meeting Planner. Washington, DC: Society for Neuroscience, 2014. Online (Published)
4. Gorgi A, **Forrest GF**, Johnson T. Electrical Stimulation Training in Persons with Spinal Cord Injury: Outcomes of Clinical Trials. American Congress Rehabilitation Medicine. October 7-11th Toronto, Canada, 2014.
5. Kozlowski A, Spungen A, **Forrest GF**, Hartigan C, Jayaraman A. Exoskeleton-Assisted Walking for Persons With Neurological Conditions, Part I: The State of the Science. Symposium. American Congress Rehabilitation Medicine. October 7-11th Toronto, Canada, 2014.
6. Kozlowski A, Spungen A, **Forrest GF**, Hartigan C, Jayaraman A, Terfillar, C. Exoskeleton-Assisted Walking for Persons With Neurological Conditions, Part II: The State of the Science. Symposium. American Congress Rehabilitation Medicine. October 7-11th Toronto, Canada, 2014.
7. Kozlowski A, Spungen A, **Forrest GF**, Hartigan C, Jayaraman A, Terfillar, C. Exoskeleton-Assisted Walking for Persons with SCI, The State of the Science. Symposium.Academy of Spinal Cord Injury Professionals August 31-September 3rd, St Louis, Missouri 2014.
8. Dyson-Hudson T, **Forrest GF**, Kirshblum S, Wu SJ. Dalfampridine and Locomotor Training for Chronic, Motor Incomplete Spinal Cord Injury Spinal Cord Med. 2014 Sep;37(5):616-49. doi: 10.1179/2045772314Y.000000000250.
9. Barrance P, Ramanujam A, Johnsen E, **Forrest GF.** (2014, July). Simulation of muscle work during hip/knee exoskeleton-assisted Gait. Presented at the 7th World Congress of Biomechanics, Boston, MA.
10. Barrance P, Ramanujam A, Johnsen E, **Forrest G**. (2014, July). Simulation of muscle work during hip/knee exoskeleton-assisted Gait. Presented at the 7th World Congress of Biomechanics, Boston, MA.
11. *Behrman A, Basso, DM; Buehner J, **Forrest GF**; Kern, M; Wojciehowski S; Schmidt Read, M.* Spinal Cord Injury SIG—Locomotor Training: Evaluation of a Standardized SCI Program Journal of Neurologic Physical Therapy: January 2014 - Volume 38 - Issue 1 - p 2–5doi: 10.1097/NPT.0000000000000024.
12. **Forrest GF**, Ramanujam A, Pierce D, Johnson E, Garbarini E, Lamb R. Muscle Atrophy After SCI And The Effect On Motor Pool Activation. Program No. 645.08/OO8. Neuroscience Meeting Planner. San Diego, CA. Society for Neuroscience, 2013. Online.
13. **Forrest GF**, Faghri P, Sisto SA, Lee S. *Electrical stimulation from basic science to clinical practice: is it evidence based?* American Congress Rehabilitation Medicine, 2013 12-16th at Disney Contemporary Resort, Walt Disney, November, 13-16th Florida, 2013.
14. Cavadini NA, Kirshblum S, Wojciehowski S, Brooks M, **Forrest GF**. Locomotor training promotes standing and walking in an individual with complete paraplegia. ASCIP. Las Vegas, September 2-4, 2013. Published in The Journal of Spinal Cord Medicine 2013 VOL. 36 NO. 5.
15. **Forrest, GF**, Lorenz DJ, Hutchinson K, Vanhiel L, Basso DM, Sisto SA, Harkema SJ. Variability patterns for walking measures: Effect of Assistive Devices. ASCIP. Las Vegas, September 2-4, 2013. Published in The Journal of Spinal Cord Medicine 542 2013 VOL. 36 NO. 5.
16. **Forrest G.F.**, Lorenz, D., Basso, M., Hutchinson, K., Hudson, L., Harkema, S.J. Recovery of trunk after spinal cord injury. Soc Neurosci, Nov., 2012. Program Number 378.03/SS19. Online (Published)
17. **Forrest G.F**, Lorenz, D., Basso, M., Hutchinson, K., Hudson, L., Harkema, S.J. Variability conundrum for walking measures. Soc Neurosci, Nov., 2012. Program Number 85.19NN9 Online (Published).
18. Faghri P., Sisto Sa., Johnston T, **Forrest GF**. The Lifespan In Spinal Cord Injury: From Pediatrics to Geratrics. Arch Phys Med Rehab. Proceedings of ACRM Conference. Vancouver, BC. October 9th-13, 2012.
19. Damcott M, Yarossi M, **Forrest GF.** *Neurophysiological Assessment Tool of Trunk Activity: Reliability and Potential to Measure Neurorecovery.* Arch Phys Med Rehab. Proceedings of 2012 ACRM Conference. Vancouver, BC. October 9th-13, 2012.Archives of Physical Medicine and Rehabilitation, Vol. 93, Issue 10, e43.Published in issue: October 2012
20. Damcott M, Pilkar R, **Forrest GF**. Efficacy of Near-Infrared Spectrometry and Electromyography to Measure Metabolic and Neuromuscular Properties During Electrical Stimulation Archives of Physical Medicine and Rehabilitation, Vol. 93, Issue 10, e45Published in issue: October 2012
21. Wojciehowski, S, Pierce, D, Kirshblum, S, Damcott, M, **Forrest GF**. Improvements in Sitting Balance after Intense Activity Based Locomotor Training with a C4 AIS B Chronic SCI: A Case Study. Proceedings of 2012 Conference ASCIP Conference. September 2-5, 2012.

22. Spungen, A, Harel, N, Forrest GF, Fineberg D, Asselin P, Kirshblum S, Research Experience with Robotic Exoskeletons Proceedings. Conference ASCIP Conference. September 2-5.2012.
23. **Forrest GF**, Hudson, L, Basso, M., Behrman, A, Harkema, SJ. Variability in Walking Measures after Spinal Cord Injury. Proceedings of 2012 Conference ASCIP Conference. September 2-5, 2012.
24. Pilkar R, Yarossi M, **Forrest GF**, "Empirical Mode Decomposition as a Tool to Remove the Function Electrical Stimulation Artifact from Surface Electromyograms: Preliminary Investigation", IEEE Engineering in Medicine and Biology Society Conference, San Diego, California, Aug 2012.

International and National Symposiums (2012-2015)

1. Johnston, T, Shields, RK, Forrest, GF, Gorgey, AS. Bone Health Post a Spinal Cord Injury: Current State of Knowledge and Evidence for Change following PT Interventions. Combined Sections Meeting. 2016. February 17-20th Anaheim, Ca, USA
2. Fyffe D, Taylor H, Basso M, **Forrest GF**. Recovery and Psychosocial Outcomes Associated with Locomotor Training and Quality of Life in Spinal Cord Injury. American Congress Rehabilitation Medicine. October 25-30th Dallas, Texas, 2015.
3. Kozlowski A, **Forrest GF** Spungen A, Hartigan C, Jayaraman A. Exoskeleton-Assisted Walking for Persons with Neurological Conditions: Clinical Application, Health and Fitness, and Personal Mobility. American Congress Rehabilitation Medicine. October 25-30th Dallas, Texas, 2015.
4. Johnson T, Gorgi A, **Forrest GF**, Shields R. Bone Health Post Spinal Cord Injury: Current State of Knowledge and Evidence for Change following a PT Intervention. Symposium Presentation Neurology Combined Sections Meeting, APTA. February, 17-20th Anaheim, CA, 2016.
5. Gorgi A, **Forrest, GF**, Johnson T. Electrical Stimulation Training in Persons With Spinal Cord Injury: Outcomes of Clinical Trials. Symposium Presentation American Congress Rehabilitation Medicine. October 7-11th Toronto, Canada, 2014.
6. Kozlowski A, Spungen A, **Forrest GF**, Hartigan C, Jayaraman A. Exoskeleton-Assisted Walking for Persons With Neurological Conditions, Part I: American Congress Rehabilitation Medicine. The State of the Science. Symposium October 7-11th Toronto, Canada, 2014.
7. Kozlowski A, Spungen A, **Forrest GF**, Hartigan C, Jayaraman A. Exoskeleton-Assisted Walking for Persons With Neurological Conditions, Part II: The State of the Science. Symposium American Congress Rehabilitation Medicine. October 7-11th Toronto, Canada, 2014.
8. Kozlowski A, Spungen A, **Forrest GF**, Hartigan C, Jayaraman A. Exoskeleton-Assisted Walking for Persons With SCI: The State of the Science. Symposium Symposium Academy of Spinal Cord Injury Professionals August 31-September 3rd, St Louis, Missouri, 2014.
9. Behrman A, Basso DM, Buehner J, **Forrest GF**, Kern M, Wojciehowski S, Schmidt Read M. Spinal Cord Injury SIG—Locomotor Training: Evaluation of a Standardized SCI Program. Symposium Presentation. Neurology Combined Sections Meeting, APTA February 6th, Las Vegas, Nevada, 2014.
10. **Forrest GF**, Faghri, P, Sisto SA, Lee S. Electrical stimulation from basic science to clinical practice: is it evidence based? Symposium Presentation American Congress Rehabilitation Medicine, 2013 12-16th. Disney Contemporary Resort, Walt Disney, November, 13-16th Florida, 2013.
11. Harkema, SJ, Fehlings M, **Forrest GF**, Schmidt-Read M. North American Clinical Trials Network (NACTN) and the neurorecovery Network: Advancing SCI Research and Translation of Evidence into Practice. ASIA 40th Anniversary Scientific Meeting. Chicago, Illinois. May6-8th, 2013.
12. Faghri P, Sisto SA, Johnston T, **Forrest GF**. The Lifespan In Spinal Cord Injury: From Pediatrics to Geratrics. Arch Phys Med Rehab. Proceedings of ACRM Conference. Vancouver, BC. October 9th-13, 2012.
13. Spungen A, Harel N, **Forrest GF**, Fineberg D, Asselin P, Kirshblum S, Research Experience with Robotic Exoskeletons. Academy of Spinal Cord Injury Professionals (ASCIP) Conference. September 2-5.2012.
14. **Forrest GF**, Hudson, L, Basso, M., Behrman, A, Harkema, SJ. Variability in Walking Measures after Spinal Cord Injury. Proceedings of 2012 ASCIP Conference. September 2-5, 2012. Published in The Journal of Spinal Cord Medicine 542 2013 VOL. 36 NO. 5

D. Research Support (2012-2015).

Ongoing Research Support.

Rehabilitation Engineering Research Centers **(RERC) Forrest (project PI)** 7/1/2015 – 12/31/2020
National Institute on Disability, Independent Living and Rehabilitation Research
Site Project: Exoskeleton and spinal cord stimulation for SCI:
We propose that the combination of interventions of the exoskeleton assisted walking (EAW) with transcutaneous lumbosacral stimulation (TLS) would increase the excitability of the cord and afferent input when training in the exoskeleton to increase lower extremity muscle firing and to functionally increase walking speed.

W81XWH-14-2-0190 Department of Defense **PI Forrest** 9/1/2014-8/30/2018

USAMRAA/CDMRP/DoD
Testosterone combined with Electrical Stimulation and Stand Retraining.
A Phase I/II prospective, randomized, double blind, controlled, multi-site clinical trial where the primary aim is to determine the neurological and neuromuscular interaction of testosterone, neuromuscular stimulation of multiple lower limb muscles and loading in individuals with sub acute to early chronic SCI who are non ambulatory. Ultimately we are interested in recovery of muscle and bone and the effect on functional motor gain for chronic SCI.

B1-2015-PP PI Harkema **Forrest (Co-I)** 3/4/2015 – 3/4/2020
Christopher Dana Reeves Foundation.
BIG Idea Project: Recovery of Autonomic control of cardiovascular and bladder function and the ability to stand and voluntary leg control movements below the level if injury with epidural stimulation
The objective of the project is to test the hypotheses related to neural control of human movement and cardiovascular function after human spinal cord injury while also obtaining knowledge for optimizing spinal cord epidural stimulation (scES) as a therapeutic intervention that can be immediately translated to larger numbers of patients who now have no treatment options for the secondary consequences of spinal cord injury.

SC140099 Department of Defense PI Bloom; **Site PI Forrest** 9/1/2015-8/30/2018
USAMRAA/CDMRP/Department of Defense
Biomarkers of Spontaneous Recovery from Traumatic Spinal Cord Injury
The objective is to test the hypothesis that levels of some inflammatory biomarkers correlate inversely with functional recovery throughout the first year after spinal cord injury (SCI). The project specific aims are to (1) identify the circulating inflammatory response in patients with SCI, (2) determine the trajectory of spontaneous functional recovery in patients with SCI, and (3) derive a predictive, multiscale model of functional recovery after SCI.

W81XWH-14-2-0170 PI Spungen – **Site PI Forrest** 9/1/2014-8/30/2017
USAMRAA/CDMRP. Department of Defense
A Randomized, Crossover Clinical Trial of Exoskeletal-Assisted Walking to Improve Mobility, Bowel Function, and Cardiometabolic Profiles in Persons with SCI"
The primary objectives of this research is to document how long it will take to reach functional gains, such as speed and distance after 36 sessions of training with these devices. Preliminary studies support the goals that walking in the exoskeletons will improve bowel function and body composition.

CSCR14ERG007 Pilkar (PI) **Forrest (Co-I)** 10/17/2014-9/16/2016
New Jersey Commission on Spinal Cord Research
Development of Signal Processing Toolbox for Assessing Neuromuscular Response during Electrical Stimulation.
The goal of this study is to develop a robust signal processing algorithm to extract EMG during ES and study the physiological significance of ES on neuromuscular properties of the stimulated muscle. The outcomes of this study will help in understanding the direct effects of ES on muscles by getting access to high quality EMG during ES and help the clinician or researcher to modify and optimize FES training paradigms based on the target muscle response. This could have a major impact on the field of spinal cord injury research and rehabilitation

Parker Hannifan **Site Forrest** 10/17/2014-9/16/2016
Indego® Exoskeleton; Assessing Mobility for Persons with Spinal Cord Injury (SCI).
*Two separate protocols are under the one title; *PH-INDO1 (FDA) and *PH-IND02 (Exploratory)
Description of Project:
The purpose of this project is to evaluate if the Indego® robotic device is both safe and effective at allowing persons with SCI who are non-ambulatory or poorly ambulatory to stand up and walk under a variety of conditions; indoor surfaces, outdoor surfaces, elevators, managing doorways, different seat heights and extended distances.

CSCR13IRG013 **Forrest (PI)** 6/17/2013-6/16/2017
New Jersey Commission on Spinal Cord Research)
Non-ambulatory SCI walk using a Robotic Exoskeleton: Effect on bone and muscle
The overall purpose of this pilot study is to assess if 5 hours per week for 20 weeks of exoskeleton-assisted walking over ground for persons with chronic SCI will positively affect the musculoskeletal system. In addition we will evlaute the human neuromuscluar and mechanic reposne to the robot.

NJCSCR13FEL009 **Forrest (Co-I)** 10/17/2014-9/16/2016
New Jersey Commission on Spinal Cord Research
Quantitative Measure of Force During Electrical Stimulation: An Exploratory Study

Non-ambulatory SCI walk using a Robotic Exoskeleton: Effect on bone and muscle
The overall purpose of this pilot study is to assess the muscle activation, 3D forces and moments generated at the knee during ES induced contraction during standing for motor complete SCI. **Mentor: Forrest GF**
Mehmed Bugrahan Bayram (PI)

H133N110020 **Forrest (Co-PI)** 10/01/2011 – 9/31/17
NIDRR Models Systems Primary Research Project
Restoring Lost Functions after Spinal Cord Injury: Combination Therapy with Dalfampridine and Locomotor Training for Persons with Chronic, Motor Incomplete Spinal Cord Injury.
The primary purpose of this National Institute on Disability and Rehabilitation Research funded project is to examine the effect of combination of Dalfampridine and Locomotor Training on walking distance and musculoskeletal system.

1R21NS095052-01A1 **Jiang T (PI) Forrest (Co-I)** 04/01/2016-3/31/201
NINDS. Major goal is to complete Longitudinal Assessment of Spinal Cord Structural Plasticity using DTI in SCI Patients

CSCR15ERG013NJC: **Jiang T (PI) Forrest (Co-I)** 6/29/2015-6/30/2017
New Jersey Commission on Spinal Cord injury
The major goal is assessing Spinal Cord Structural Changes using Diffusion Tensor Iimaging in Patients with Incomplete Traumatic Spinal Cord Injury

191152 **Forrest (PI)** 7/1/2014 – 1/31/2015
Craig H Neilson Foundation
Activity-Dependent Rehabilitation Model to improve Bone and Muscle after SCI.
Note – this is a no cost extension of the original grant ($250,000)
The purpose is to assess the musculoskeletal gains in individuals with subacute to chronic SCI, with bone mineral density as the primary outcome variable and volumetric measures of bone, bone markers for reabsorption and absorption, muscle volume and muscle expression of PGC-1α as secondary outcome measures.

143298 **Forrest (Co-PI)** 01/01/2007 – 12/31/2017
NIDRR
Advanced Rehabilitation Research and Training Center (ARRTC) on Neuromusculoskeletal Rehabilitation Post-Doctoral Training Grant.
The purpose of this NIDRR funded ARRT project is to provide research training and experience at an advanced level to individuals with doctorates or similar advanced degrees who have clinical or other relevant experience.

SC090246 **Behrman (PI) Forrest (Co-I)** 10/1/2012-9/30/2016
Department of Defense/University of Florida
A new measure of neurological and behavioral recovery after SCI
The major goal of this project is to Assess the responsiveness of the Phase System for evaluating recovery from SCI over the period of 1) in-patient rehabilitation (sub-acute SCI) receiving usual care and 2) outpatient rehabilitation (chronic SCI) while receiving an intense, activity-based therapy.

07-3063-SCR-E-0 **Forrest (Co-PI)** 01/01/207 – 1/31/2017
Center For Disease Control and Christopher Dana Reeves Foundation
NeuroRecovery Network grant.
The major goal of this project is to develop specialized centers that provide standardized activity-based therapy care based on current scientific and clinical evidence for people with SCI and other selected neurological disorders.

OMB No. 0925-0001 and 0925-0002 (Rev. 10/15 Approved Through 10/31/2018)

BIOGRAPHICAL SKETCH

Provide the following information for the Senior/key personnel and other significant contributors.
Follow this format for each person. **DO NOT EXCEED FIVE PAGES**.

NAME: BAUMAN, William A, MD

eRA COMMONS USER NAME (credential, e.g., agency login): WBAUMAN

POSITION TITLE: Professor of Medicine and Rehabilitation Medicine; Director, Center for the Medical Consequences of SCI, Co-Investigator

EDUCATION/TRAINING

INSTITUTION AND LOCATION	DEGREE	Completion Date	FIELD OF STUDY
Harvard College, Boston, MA	B.A.	06/1972	English
State University of New York, Downstate College of Medicine, New York, NY	M.D.	06/1976	Medicine

2 A. Personal Statement

Since 1990, as Director of the Spinal Cord Damage Research Center, my career has been directed to better define the medical complications of spinal cord injury (SCI). Once these adverse conditions have been more clearly defined, our investigators have intervened to reduce their detrimental impact or to prevent their occurrence. Early in my career, I first described the high prevalence of diabetes, insulin resistance, and adverse changes in lipid profiles in the SCI population, as well as the rapid loss of bone after acute paralysis and subsequent immobilization osteoporosis. The success of my research and my continued dedication to addressing the needs of individuals with SCI led to my establishing the VA RR&D's National Center of Excellence for the Medical Consequences of SCI in 2001, and I have served as the Center's Director since its inception. I was Chairman of the VA Cooperative Study entitled "Anabolic Steroid Therapy on Pressure Ulcer Healing in Persons with Spinal Cord Injury (CS #535)," with the primary manuscript published in the Annals of Internal Medicine. Currently, I am Co-Chairman of a VA Cooperative Study entitled "Exoskeletal-Assisted Walking in Persons with SCI: Impact on Quality of Life (CS #2003)."

My efforts have resulted in over 300 peer-reviewed papers, book chapters, and review articles, which have led to nationwide changes in the care of persons with SCI. My work has been honored with multiple awards and invited lectures in the fields of endocrinology and SCI Medicine and Rehabilitation Medicine: Excellence Award from the American Paraplegia Society for outstanding leadership and accomplishments in SCI health care in 2002; Paul B. Magnuson Award from the VA's RR&D Service, its highest service award, in 2005; the 31st G. Heiner Sell Memorial Lectureship at the Annual Scientific Meeting of the American Spinal Injury Association in 2012; the Donald Monro Lecture at the 2013 Annual Meeting of the American Society of Spinal Cord Injury Professional; the prestigious Samuel J. Heyman Service to America Medal in Science and Environment in 2014.

3 B. Positions and Honors

3.1 Positions and Employment

1982 – 1987	Associate Professor of Medicine, Albert Einstein College of Medicine, Bronx, NY
1983 – 1985	Attending Consultant, Department of Medicine, VA Medical Center, Bronx, NY
1985 – 1989	Physician/Research Associate, Solomon A. Berson Research Laboratory, VA Medical Center, Bronx, NY
1987 – 1989	Associate Professor of Medicine and Rehabilitation, Mount Sinai School of Medicine, New York, NY
1989 – 2003	Director, Spinal Cord Damage Research Center, Mount Sinai Medical Center, New York and VA Medical Center, Bronx, NY
1996 – Present	Professor of Medicine, Mount Sinai School of Medicine, New York, NY
1996 – Present	Professor of Rehabilitation Medicine, Mount Sinai School of Medicine, New York, NY
2001 – Present	Director, VA Rehabilitation Research & Development Center of Excellence for the Medical Consequences of Spinal Cord Injury, James J. Peters VA Medical Center, Bronx, NY

3.2 Other Experience and Professional Memberships

1976 – 1977	Medical Internship, New York University Medical Center, New York, NY
1977 – 1979	Medical Residency, Montefiore Hospital & Medical Center, Bronx, NY
1979 – 1980	Endocrine Fellowship, VA Medical Center, Bronx, NY
1980 – 1982	Endocrine Fellowship, Montefiore Medical Center, Bronx, NY
1982 – 1985	NIH SERCA Recipient, Attending, Departments of Medicine and Endocrinology & Clinical Sciences, Montefiore Medical Center, Bronx, NY

3.3 Honors

1972	Honors graduate in English Literature, Harvard University
1982	Recipient of NIH Special Emphasis Research Career Award
1994	Excellence in Medical Research, Medical Service, VA Medical Center, Bronx, NY
2001	William Dock Award for outstanding teaching ability in Internal Medicine/Endocrinology
2002	Excellence Award in Research (American Paraplegia Society)
2005	Paul B. Magnusson Award, VA RR&D Service
2014	Medalist, Samuel J. Heyman Service to America Award, Science & Environment

4 C. Contribution to Science

1. Osteoporosis and fractures present a major problem for persons with SCI. My contributions include defining calcium metabolism and bone disease in persons with SCI. Our publications first suggested a high prevalence of vitamin D deficiency in persons with SCI and proposed an approach for vitamin D replacement therapy. Despite literature that suggested a value to bisphosphonate therapy in those with SCI, possibly because of the work conducted in those with varying completeness of lesion, our work has demonstrated the limited efficacy of bisphosphonates administration in persons with acute complete motor SCI, necessitating the search for more effective therapeutic approaches. Our work in monozygotic twins, discordant for SCI, has suggested that bone loss continues for decades after initial injury, a new and controversial finding. We have shown that bone mass below the level of lesion is directly associated to body fat, and also directly correlated to the serum estradiol levels. Our group has provided evidence of the cellular, biochemical, and molecular effects of paralysis due to SCI or nerve transaction on bone.
   a. Bauman WA, Spungen AM, Schwartz E, Wang J, Pierson RN Jr. (1999) Continuous Loss of Bone in Chronic Immobilization: A Monozygotic Twin Study. *Osteoporos Int*. 10:123-127.
   b. Bauman WA, Spungen AM, Wang J, Pierson RN, Schwartz E. (2006). Relationship of Fat Mass and Serum Estradiol with Lower Extremity Bone in Persons with Chronic Spinal Cord Injury. *Amer J Physiol Endocrinol Metab*. 290(6):E1098-103.
   c. Bauman WA, Cardozo C. (2014). Osteoporosis in Individuals with Spinal Cord Injury. *JM R*. S1934-1482(14):1358-1366.
   d. Bauman WA, Cirnigliaro CM, LaFountaine MF, Kirshblum SC, Spungen AM. (2015). Zoledronic Acid Administration Failed to Prevent Bone Loss at the Knee in Persons with Acute Spinal Cord Injury: An Observational Cohort Study. *J Bone Mineral Metab*. 33(4): 410-421.

2. Although it would appear intuitive that individuals who have adverse body composition and reside at the lowest end of the activity spectrum would have metabolic problems which predispose to cardiovascular disease, prior to our group's entrance to the field, little had been reported in the literature. My contribution has been to be the first investigator to systematically study carbohydrate and lipid metabolism in persons with SCI and suggest that the abnormalities observed would be anticipated to predispose to premature cardiovascular disease. Prior to this work, it was unclear that persons with SCI had disorders of carbohydrate metabolism, which has since been characterized by a high prevalence of carbohydrate intolerance and diabetes mellitus. The finding of low high-density lipoprotein (HDL) cholesterol in those with SCI was observed by our group and subsequently confirmed by others. By nuclear medicine technology and electron beam computerized tomography, publications demonstrated the likelihood of premature atherosclerotic disease in those with SCI. Recently, we have reported on the blunted action of insulin on the sublesional microvascular.
   a. Bauman WA, Spungen AM. *(*1994). Disorders of Carbohydrate and Lipid Metabolism in Veterans with Paraplegia or Quadriplegia: A Model of Premature Aging. *Metabolism*. 43:749-756.
   b. Bauman WA, Adkins RH, Spungen AM, Herbert R, Schechter C, Smith D, Kemp B, Waters RL. (1999). Is Immobilization Associated with an Abnormal Lipoprotein Profile? Observations from a Diverse Cohort. *Spinal Cord*. 37:485-493.
   c. Bauman WA, Adkins RH, Spungen AM, Waters RL. (1999). The Effect of Residual Neurological Deficit on Oral Glucose Tolerance in Persons with Chronic Spinal Cord Injury. *Spinal Cord*. 37:765-771.
   d. La Fountaine M, Rosado Rivera D, Radulovic M, Bauman WA. (2013). The Hemodynamic Actions of Insulin are Blunted in the Sub-lesion Microvasculature of Healthy persons with Spinal Cord Injury. *American Journal of Physical Medicine & Rehabilitation.* 92(2): 127-135.

3. Persons with SCI immediately lose muscle and gain fat after injury. Our contribution to body composition in persons with SCI has been to compare various methodologies to determine body adiposity, develop or apply innovative methodologies, define body composition changes after acute and in chronic injury, and more clearly delineate the relationship of body composition to metabolic derangements. A portion of this work, which was performed in monozygotic twins, one in each pair discordant for SCI, and in cross-sectional studies that have served to define changes in soft tissue mass over decades of life in persons with SCI, has improve our general knowledge in this area of study. The loss of muscle in those with chronic SCI occurs at an accelerated rate both above and below the level of lesion, suggesting a global, or systematic hormonal, process. Depressed levels of anabolic hormones (testosterone and growth hormone/ insulin-like growth factor) may partially explain the general adverse changes in soft tissue body composition in individuals with chronic SCI, which we demonstrated to be depressed in younger individuals with SCI. In our preclinical articles, the influence of androgens on muscle mass and signaling pathways after SCI or nerve transection has been described, as well as the antagonistic effect of androgens on the catabolic effect of glucocorticoids on muscle.
   a. Spungen AM, Wang J, Pierson RN Jr, Bauman WA. (2000).Soft Tissue Body Composition Differences in Monozygotic Twins Discordant for Spinal Cord Injury. *J Appl Physiol*. 88:1310-1315.
   b. Spungen AM, Adkins RH, Stewart CA, Wang J, Pierson RN Jr, Waters RL, Bauman WA. (2003).Factors Influencing Body Composition in Persons with Spinal Cord Injury: A Cross-sectional Study. *J Appl Physiol*. 95(6):2398-407.
   c. Bauman WA, Spungen AM, Flanagan S, Zhong YG, Alexander LR, Tsitouras PD. (1994). Blunted Growth Hormone Response to Intravenous Arginine in Subjects with a Spinal Cord Injury. *Horm Metab Res*. 26:149-153.
   d. Bauman WA, La Fountaine MF, Spungen AM. (2014). Age-related Prevalence of Low Testosterone in Men with Spinal Cord Injury. *Journal of Spinal Cord Medicine*. 37(1): 32-39.

4. Other than some of my above noted contributions to the endocrinology & metabolism of persons with SCI, my contribution to Spinal Cord Medicine have been wide in scope in both the clinical and pre-clinical areas. In clinical medicine, my publications have been in the following areas: GI motility of the esophagus, stomach, small intestine, and, especially, the colon, with interventions to improve colonic motility and evacuation, including the novel drug combination of neostigmine plus glycopyrrolate, and strategies to improve cleansing preparation for elective colonoscopy; identifying for the first time obstructive airway disease in persons with SCI and interventions to improve function, defining restrictive airway disease in persons with complete motor SCI and strategies to improve respiratory muscle strength; defined cardiovascular autonomic dysregulation in persons with SCI and interventions to improve hemodynamics, as well as the association of cognitive deficits associated with hypotension; pressure ulcer energy requirements, healing, and intervention to heal the wound. Our work has reported the mechanics and benefit of exoskeletal-assisted ambulation.
   a. Bauman WA, Korsten MA, Radulovic M, Gregory J. Schilero GJ, Jill M. Wecht, JM, Spungen AM. (2012). 31st G. Heiner Sell Lectureship: Secondary Medical Consequences of Spinal Cord Injury. *Top Spinal Cord Rehabil* .18 (4):354-378.
   b. Wecht JM, Bauman WA. (2013). Decentralized Cardiovascular Autonomic Control and Cognitive Deficits in Persons with Spinal Cord Injury. *J Spinal Cord Med.* 36:74-81.
   c. Bauman WA, Spungen AM, Collins JF, et al. (2013). A Randomized Clinical Control Trial of Anabolic Steroid Therapy on Pressure Ulcer Healing in Persons with Spinal Cord Injury. *Annals of Internal Medicine.* 158(10):718-726.
   d. Schilero GJ, Radulovic M, Lesser M, Bauman WA. (2014). A Center's Experience: Pulmonary Function in Spinal Cord Injury. *Lung.* 192(3):339-46.

4.1 Complete List of Published Work in MyBibliography:
http://www.ncbi.nlm.nih.gov/sites/myncbi/18Wf9J7w8ZFAN/bibliography/47313079/public/?sort=date&direction=descending

D. Research Support

Ongoing Research Support

VA RR&D #B9212-C Bauman (PI) 07/01/11-06/30/16
National Center Grant
$450,000
Center of Excellence for the Medical Consequences of Spinal Cord Injury
To improve health and quality of life in five major program areas: (1) endocrine & metabolic, (2) pulmonary, (3) GI, (4) cardiovascular autonomic, and (5) molecular-musculoskeletal.
Role: Director/Principal Investigator

Grant # 297267 Bauman (PI)
07/01/14 – 06/30/17
Craig H. Neilsen Foundation
$598,818
Title: Prevention of Bone Loss after Acute Spinal Cord Injury
Denosumab will be tested to prevent bone loss in persons with acute/subacute SCI.
Role: PI

VA RR&D #B1392-P Bauman (PI)
07/014 – 06/16
Merit Review
$199,957
Title: Insulin Resistance and Microvascular Blood Flow in Spinal Cord Injury
In healthy persons with chronic SCI, to determine the effect of insulin to induce vasodilatation of the microvasculature above and below the level of lesion compared to that of heat or other medications.
Role: PI

VA CSP #2003 Bauman & Spungen (Co-Chairman) 10/01/15-9/30/20
VA CSR&D
$22,000,000
Exoskeletal-Assisted Walking in Persons with SCI: Impact on Quality of Life
To demonstrate that Veterans with chronic SCI plus an exoskeletal-assisted walking device in their home and community environments will have clinically meaningful improvements in QOL measures, including those of the MCS/VR-36 and SCI-QOL bladder, bowel, and pain item banks.
Role: Co-Investigator

Federal #B1313-R Qin (PI)
10/01/14 – 9/30/18
VA RR&D Service $885,291
Title: Sclerostin Antagonism and the Osteocyte's Role: Prevention of Bone Loss
To determine the ability of anti-sclerostin antibody to preserve bone integrity after acute SCI, and to test whether impairment of osteocyte function is one mechanism by which SCI causes bone loss, and whether restoration of normal osteocyte function after anti-sclerostin antibody can prevent or reverse bone loss.
Role: Co-Investigator

VA RR&D #B8048R Qin (PI)
09/01/13 – 08/31/16
IIR Merit Review
$621,488
Title: FES and Androgens in Bone Loss after SCI: Synergistic Effects and Mechanisms
In a rat model of acute SCI, to determine the ability of mechanical intervention (functional electrical stimulation) or testosterone administration to reduce or prevent bone loss.
Role: Co-Investigator

CDMRP #11235809 Forrest (PI)
9/01/14-8/30/17
Department of Defense CDMRP
$984,976
Title: Testosterone Combined With Electrical Stimulation & Standing: Effect on Muscle and Bone
In collaboration with Kessler, to test whether standing with or without muscle electrical stimulation with testosterone/placebo will improve muscle mass and bone mass.
Role: Co-PI

#CSCR13IRG013 Forrest (PI)
05/17/13 – 03/30/16
New Jersey State Commission
$239,193
Title: Non-ambulatory SCI Walk Using a Robotic Exoskeleton: Effect on Bone and Muscle
In collaboration with Kessler, to test whether exoskeletal ambulation improves muscle and bone.
Role: Co-Investigator

Grant # 284196 Wecht (PI)
03/01/14 – 02/28/17
Craig H. Neilsen Foundation
$593,179
Title: Blood Pressure, Cerebral Blood Flow and Cognition in SCI
To assess the relationships among systemic blood pressure, cerebral blood flow, & cognition in tetraplegia.
Role: Co-investigator

CSCR13IRG018 Wecht & Chiaravolloti (PIs)
06/01/13 – 05/30/16
New Jersey Commission on Spinal Cord Research $596,954
Title: Impact of Age on Cardiovascular, Cerebral Vascular and Cognitive Health in Spinal Cord Injury
To determine the relationships among blood pressure, cerebral blood flow, and cognition will be determined in persons with spinal cord injury over a range of ages and compared to older, able-bodied individuals.
Role: Co-Investigator

#B1925-P La Fountaine (PI)
06/2015 - 05/2017
VA RR&D SPiRE
$200,000
Title: An Open-Label Safety and Efficacy Trial of Fenofibrate in Persons with SCI
To test the use fenofibrate, a PPAR-α agonist, to lower concentrations of triglyceride-rich lipoproteins and that of other lipid particles in persons with SCI.
Role: Co-Investigator

1 I21 RX001734-01A1 Handrakis
06/01/15 – 05/31/17
RR&D Service
$196,289
Title: Effect of Heat Exposure on Cognition in Persons with Tetraplegia
To determine the effect of mild hyperthermia on the ability of persons with tetraplegia to perform cognitive tasks will be determined.
Role: Co-Investigator

1 I21 RX001734-01A1 Handrakis
06/01/15 – 05/31/17
RR&D Service
$168,274
Title: Thermoregulation and Cognition during Cool Ambient Exposure in Tetraplegia
To determine the change in core body temperature and cognitive performance (attention, memory, processing speed, executive function) in persons with tetraplegia.
Role: Co-Investigator

1 I21 RX001915-01 Korsten
06/01/15 – 05/31/17
RR&D Service
$193,394
Title: Bowel Biofeedback Training to Improve Bowel Function in Individuals with SCI
To determine the functional bowel phenotype based on anorectal high-resolution manometry findings in individuals with incomplete motor SCI, and to compare these findings with findings of able-bodied individuals with normal bowel function.
Role: Co-Investigator

1 I21 RX001910-01 Schilero
08/01/15 – 07/31/17
RR&D Service
$193,849
Title: The Effect of an Oral Beta-2 Agonist on Respiratory Muscle Strength in SCI
To determine in individuals with cervical (C3-C8) and high thoracic (T1-T6) SCI who have moderate to severe respiratory muscle weakness (baseline MIP < 90 cmH2O) whether 16-weeks of treatment with an oral beta-2 agonist improves surrogate indices of respiratory muscle strength and cough.
Role: Co-Investigator